

1. A method for treating a patient having a condition affecting at least one layer of skin comprising administering in situ a physiologically acceptable formulation containing at least one enzyme selective for a layer of skin affected by said condition in an amount and for a duration effective to remove said layer and treat said condition.
2. The method of claim 1 wherein said layer of skin is selected from the group consisting of an epidermal layer, a dermal layer, a subcutaneous layer, and combinations thereof.
3. The method of claim 1 wherein said enzyme is a hydrolase.
4. The method of claim 3 wherein said hydrolase is selected from the group consisting of esterases, glycosidases, proteases, phosphatases, thiolases, phospholipases, amidases, ceramidases, lipases, deaminases, nucleases and combinations thereof.
5. The method of claim 1 wherein said enzyme is selected from the group consisting of trypsin, chymotrypsin, papain, bromelain, dispase, thermolysin, ceramidase, lipase, glycosidase, deoxyribonuclease, ribonuclease and combinations thereof to treat an epidermal layer.

6. The method of claim 1 wherein said enzyme is selected from the group consisting of collagenase, elastase, and combinations thereof to treat a dermal layer.

7. The method of claim 1 wherein said enzyme is a lipase to treat a subcutaneous layer.

8. The method of claim 1 where the condition is selected from the group consisting of neoplasms, pigmentary disorders, infectious disorders, follicular disorders, hyperkeratotic disorders, inflammatory disorders, vascular disorders, photo-aging disorders, deposition disorders, connective tissue disorders, and cutaneous cystic disorders.

9. The method of claim 1 wherein the enzyme is selected from the group consisting of trypsin, chymotrypsin, papain, collagenase, pepsin A, elastase, exopeptidases, aminopeptidases, endopeptidases, bromelain, chymotrypsin C, metridin, trypsin, thrombin, plasmin, enteropeptidase, alpha-lytic endopeptidase, prolyl oligopeptidase, brachyurin, plasma kallikrein, tissue kallikrein, pancreatic elastase, leukocyte elastase, chymase, cerevisin, hypodermin C, endopeptidase La, alpha-renin, leucyl endopeptidase, tryptase, kexin, subtilisin, oryzin, endopeptidase K, thermomycolin, thermitase, endopeptidase So, tissue plasminogen activator, pancreatic endopeptidase E, pancreatic elastase II, urine plasminogen activator, cathepsin B, facain, chymopapain, asclepain, clostripain, streptopain, actinidain, cathepsin L, cathepsin H, calpain, cathepsin T, glycyl endopeptidase, cathepsin S, caricain,

- ananain, stem bromelain, fruit bromelain, legumain, histolysin, pepsin B, gastricsin, chymosin, cathepsin D, retropepsin, aspergillopepsin I, aspergillopepsin II, penicillopepsin, rhizopuspepsin, endothiapepsin, mucorpepsin, candidapepsin, saccharopepsin, rhodotorulapepsin,
- 5 physaropepsin, acrocylindropepsin, polyporopepsin, pycnoporopepsin, scytalidopepsin A, scytalidopepsin B, xanthomonoapepsin, pseudomonapepsin, cathepsin E, atrolysin, microbial collagenase, leucolysin, interstitial collagenase, neprilysin, matrix metalloproteinases dispase, thermolysin, V8 protease, ribonuclease, deoxyribonuclease. and combinations thereof.

10. The method of claim 1 wherein said administering is selected from the group consisting of topical application, injection, and combinations thereof.

11. A composition comprising at least one protease selected from the group consisting of trypsin, chymotrypsin, papain, bromelain, dispase, thermolysin, V8 protease, and combinations thereof at a concentration in the range of about  $1 \times 10^{-5}\%$  w/v to about  $10\%$  w/v in a pharmaceutically acceptable formulation to selectively effect an epidermal layer of skin.
12. The composition of claim 11 wherein said protease is selected from the group consisting of naturally occurring proteases, synthetic proteases, and combinations thereof.
13. The composition of claim 11 wherein the concentration of protease is in the range of about  $1 \times 10^{-4}\%$  w/v to about  $10\%$  w/v.
14. The composition of claim 11 wherein the concentration of protease is in the range of about  $0.1\%$  w/v to about  $3.0\%$  w/v.
15. The composition of claim 11 wherein the formulation is selected from the group consisting of creams, ointments, lotions, liniments, gels, solutions, suspensions, pastes, sticks, sprays, beads, spheres, microbeads, microspheres, liposomes, and combinations thereof.
16. The composition of claim 11 further containing a co-additive selected from the group consisting of exfoliants, immunomodulating drugs, cytotoxic drugs and combinations thereof.

17. The composition of claim 16 wherein said exfoliant is selected from the group consisting of ethylenediaminetetracetic acid (EDTA), ethylene glycol-bis ( $\beta$ -aminoethyl ether)-N,N,N',N'-tetra acetic acid (EGTA), salicylic acid, lactic acid, alpha-hydroxy acids, beta-hydroxy acids, urea and combinations thereof.

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18. The composition of claim 16 wherein said immunomodulating drug is selected from the group consisting of glucocorticoids, tacrolimus, cyclosporin, interferon, ascomycin (SDZ ASM 981), imiquimod, or any of their respective derivatives and their combinations thereof.

19. The composition of claim 16 wherein said cytotoxic agent is selected from the group consisting of podophyllin, podophylox, cantharadin, and combinations thereof.

20. A topically applied composition for treating a patient having a skin condition affecting at least one epidermal, and/or dermal layer, and/or subcutaneous layer comprising a hydrolase in a pharmaceutically acceptable formulation, said enzyme in an amount in the range of about  $1 \times 10^{-5}\%$  by weight to about 10% by weight of said formulation.

21. The composition of claim 20 wherein said enzyme is a hydrolase selected from the group consisting of esterases, glycosidases, proteases, phosphatases, thiolases, phospholipases, amidases, ceramidases, lipases, deaminases, nucleases and combinations thereof.

22. The composition of claim 21 wherein said hydrolase is selected from the group consisting of naturally occurring hydrolases, synthetic hydrolases, and combinations thereof.

23. The composition of claim 21 wherein said protease is selected from the group consisting of collagenases, trypsin, papain, bromelain, streptokinase, chymotrypsin, chymotrypsin C, elastases, exopeptidases, endopeptidases, metridin, thrombin, plasmin, enteropeptidase, alpha-lytic endopeptidase, prolyl oligopeptidase, brachyurin, plasma kallikrein, tissue kallikrein, pancreatic elastase, leukocyte elastase, chymase, cerevisin, hypodermin C, endopeptidase La, alpha-renin, leucyl endopeptidase, tryptase, kexin, subtilisin, oryzin, endopeptidase K, thermomycolin, thermitase, endopeptidase So, tissue plasminogen activator, pancreatic endopeptidase E, pancreatic elastase II, urine plasminogen activator, cathepsin B, papain, ficain,

chymopapain, asclepain, clostripain, streptopain, actinidain, cathepsin L,  
cathepsin H, calpain, cathepsin T, glycyl endopeptidase, cathepsin S, caricain,  
ananain, stem bromelain, fruit bromelain, legumain, histolysain, pepsin A,  
pepsin B, gastricsin, chymosin, cathepsin D, retropepsin, aspergillopepsin I,  
5 aspergillopepsin II, penicillopepsin, rhizopuspepsin, endothiapepsin,  
mucorpepsin, candidapepsin, saccharopepsin, rhodotorulapepsin,  
physaropepsin, acrocylindropepsin, polyporopepsin, pycnoporopepsin,  
scytalidopepsin A, scytalidopepsin B, xanthomonoapepsin, pseudomonapepsin,  
cathepsin E, atrolysin, microbial collagenase, leucolysin, interstitial collagenase,  
10 neprilysin, matrix metalloproteinases, dispase, thermolysin, V8 protease and  
combinations thereof.

25. The method of claim 24 wherein said protease is selected from the group consisting of trypsin, papain, bromelain, dispase, thermolysin, and combinations thereof.



26. A method to treat skin comprising providing a composition containing a protease in a biologically acceptable formulation in an amount and formulation to selectively remove at least one dermal layer containing a skin condition to thereby treat said skin.

27. The method of claim 26 wherein said composition is provided by an administration method selected from the group consisting of topical, injection, and combinations thereof.

28. The method of claim 26 wherein said protease is selected from the group consisting of collagenases, elastases, and combinations thereof.

Case	Age	Sex	Duration	Site	Pathology	Response	Survival
1	65	M	10 years	Rectum	Adenocarcinoma	CR	10 years
2	58	F	5 years	Colon	Adenocarcinoma	CR	5 years
3	72	M	15 years	Rectum	Adenocarcinoma	CR	15 years
4	60	F	8 years	Colon	Adenocarcinoma	CR	8 years
5	68	M	12 years	Rectum	Adenocarcinoma	CR	12 years
6	55	F	7 years	Colon	Adenocarcinoma	CR	7 years
7	70	M	18 years	Rectum	Adenocarcinoma	CR	18 years
8	62	F	9 years	Colon	Adenocarcinoma	CR	9 years
9	66	M	11 years	Rectum	Adenocarcinoma	CR	11 years
10	59	F	6 years	Colon	Adenocarcinoma	CR	6 years

30. A method to target skin treatment of an affected area comprising providing to said affected area a composition containing at least one enzyme in an amount and formulation effective to selectively target skin removal in said affected area.

31. The method of claim 30 wherein said affected area is selected from the group consisting of epidermis, dermis, subcutaneous layer, and combinations thereof.

32. The method of claim 30 wherein said affected area is selected from the group consisting of epidermis, dermis, subcutaneous layer, and combinations thereof.

32. A method of treating aging in at least one layer of skin comprising providing a protease-containing biologically acceptable composition to an outermost layer of affected skin in an amount and formulation to selectively target said affected skin layers.

33. The method of claim 32 wherein said signs are selected from the group consisting of xerosis, rhytids, loss of skin tone, acitinic damage, fine lines, dyspigmentation, and combinations thereof.

34. A method for treating a condition affecting skin comprising applying a composition to the affected skin, the composition containing at least one enzyme at a concentration selective for regulating depth of skin treatment and applied to an area selective for regulating a radial surface of skin treatment.
35. The method of claim 34 wherein the enzyme is a protease.
36. The method of claim 34 wherein the composition is topically applied.
37. The method of claim 34 wherein the composition comprises a protease and is topically applied.
38. The method of claim 34 wherein the composition is applied one time.
39. The method of claim 34 wherein the enzyme is a protease to treat an epidermal layer.
40. The method of claim 34 wherein a relatively short duration of exposure and a relatively low enzyme concentration is used to treat a condition affecting an epidermal layer.

41. The method of claim 34 wherein a relatively long duration of exposure and a relatively high enzyme concentration is used to treat a condition affecting a dermal layer.

41. The method of claim 34 wherein a relatively long duration of exposure and a relatively high enzyme concentration is used to treat a condition affecting a dermal layer.